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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,955	07/07/2003	Hirohiko Tsuzuki	Q76105	4760

23373 7590 09/07/2005

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EXAMINER	
SINGH, SATYENDRA K	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 09/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/612,955	TSUZUKI ET AL.	
	Examiner	Art Unit	
	Satyendra K. Singh	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-15 and 17-19* is/are pending in the application.

4a) Of the above claim(s) *1-11, ~~16~~ and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-15 and 17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 July 2003 and 02 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *07/07/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group IV (claims 17-19) in the reply filed with the office on Aug. 11th 2005 is acknowledged.

Claims 1-11, 16, and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected groups of inventions, there being no allowable generic or linking claim. Election was made **without traverse** in the reply filed on Aug. 11th 2005.

Applicant's assertion that claim 20 depends from claim 12 and 19 and therefore should be examined with the linking claims 12-15, is however, not applicable. The inventions of Group IV (claims 17-19) use the carrier for cell culture as recited in claim 12, and therefore, claims 12-15 will be examined on their merit. However, the invention of Group V (claim 20) is a cell culture (product) obtained by the method of claim 19 but the product such as claimed can be obtained by using other cell culture carriers known to the art and therefore, does not merit further examination, hereafter.

Claims 12-15 and 17-19 are examined on their merits hereafter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Hara et al (U.S. Patent 6,821,107 B1, [A]).

Claim 18 is drawn to **a cell culture (product)** obtained by the method according to claim 17 that uses the carrier for cell culture as claimed in claim 12.

As per MPEP § 2113 *"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).*

Hara et al [A] teaches such a cell culture (a layer of fibroblast cells cultured on a cell culture carrier comprising an alginate gel layer coated with collagen) obtained by the method for culturing cells (see Hara et al, column 7-8, example 2-3, in particular) which are the same as claimed in the instant invention irrespective of the changes in the carrier for cell culture made in the present application. The presence of chitosan layer in between collagen and alginate gel layers may provide added benefits (such as extra reinforcement, etc.) for lamination and other related procedures, but will not significantly change the cultured product as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 12-15 and 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hara et al (U.S. Patent 6,821,107 B1, [A]) in view of Huguet & Dellacherie [U] and Clapper et al (U.S. Patent 5,512,474 [B]).

Linking claims 12-15 are drawn to a carrier for cell culture that comprises a water-containing gel comprising alginate or alginate/polylysine, wherein a surface of the carrier is coated with collagen, and wherein the collagen and the water-containing gel containing alginate are intermediated by a layer of chitosan, and wherein the alginate containing carrier for cell culture is formed on a porous membrane.

The carrier for cell culture, as claimed in the present invention, is formed on a porous membrane and comprises of a layer of alginate gel coated with collagen

containing an intermediate layer of chitosan between alginate gel layer and collagen coating, and may enable culture (as well as visualization) of mammalian cells (anchorage-dependent or adherent cultures) on the collagen layer using various culture media and conditions used for standard cell culture.

Claims 17-19 are drawn to a method for culturing cells and a cell culture obtained by such method using the carrier for cell culture as claimed in claim 12.

Hara et al [A] teach a carrier for cell culture comprising an alginate gel layer (calcium alginate as claimed in the instant claim 13) formed on a porous membrane (as claimed in the instant claim 15) having an extracellular matrix component gel layer (made of collagen) or extracellular matrix component sponge layer formed on the alginate gel layer (see Hara et al, abstract, fig. 1 and 2, summary of the invention, and example 1, in particular). Hara et al [A] also teach a method for culturing cells, a method for producing cell culture, and a cell culture obtained by the methods using the carrier for cell culture where the cell layer is formed on the extracellular matrix component gel layer or extracellular matrix component sponge layer or on the alginate gel layer by the method step of allowing the cells to grow and form a cell layer on the surface of the carrier for cell culture (see Hara et al, example 2, in particular). In addition, the alginate gel layer is solubilized using chelating agent to exfoliate cell layer from the porous membrane, and the exfoliated cell layer is further laminated on another cell layer on a carrier providing a method of forming a structure having multiple cell layers (see Hara et al, abstract, fig 1 & 2, summary, and examples 2-3, in particular).

However, a carrier for cell culture where the collagen layer is bound to a surface of the water-containing gel (comprising alginate) by means of **chitosan as an intermediate layer** is not taught by Hara et al [A].

Huguet & Dellacherie [U] teach a microcapsule (suitable for microencapsulation of biological materials, including cells) comprising calcium alginate beads that are coated with chtosan as an outermost layer in order to study the rate of release of biological materials such as proteins, and dextran (having different molecular weights) from the encapsulated beads (see Huguet & Dellacherie, abstract, introduction, methods, pages 745-746, in particular and references therein).

In addition, Clapper et al [B] teach a cell culture system comprising a support material providing a surface for the attachment of cells (for the purpose of anchorage-dependent cell culture) comprising a stable combination of positively-charged molecule (chitosan) and cell adhesion factor (collagen) (see Clapper et al, abstract, summary, column 3-4, in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the carrier for cell culture of Hara et al [A] (and therefore, the methods steps for culturing and producing the cell culture using such modified carrier) comprising an alginate gel layer formed on a porous membrane which is further coated with a collagen layer, such that the collagen gel layer is bound to a surface of alginate by means of a polycationic polysaccharide (such as chitosan) as explicitly taught by Huguet & Dellacherie [U] and Clapper et al [B].

The person of ordinary skill in the art would have been motivated to make that modification in the carrier for cell culture (and therefore, the methods steps dependent on it) by incorporating an intermediate layer containing chitosan (which is bound to the layers of collagen and water-containing gel containing alginate) because -1) Huguet & Dellacherie disclose the benefits of coating calcium alginate with chitosan in order to providing strength and reinforcement to the water-containing gel (alginate gel) layer (see Huguet & Dellacherie, page 745, abstract and introduction, in particular); and -2) Clapper et al [B] explicitly disclose the benefits of using polycationic or positively charged molecule (chitosan or polylysine) in combination with cell adhesion factor (collagen, etc.) bound to the surface of a cell culture support of a bioreactor to improve cell attachment and stabilize cell growth (see Clapper et al, abstract, summary, and column 3-4, and examples, in particular).

One of ordinary skill in the art would have had a reasonable expectation of success when modifying the carrier for cell culture (and therefore, the attendant method steps using such modified carrier for cell culture) as taught by Hara et al by incorporating an intermediate layer of chitosan (between the layers of water-containing alginate gel and collagen) as taught by Huguet & Dellacherie and Clapper et al because the prior arts explicitly teach the method steps involved in the preparation and use of chitosan for coating the alginate gel layer as well as the method for the providing coating of chitosan and collagen on a cell culture support system for obtaining enhanced cell attachment in anchorage-dependent cell culture systems.

Although, the shape of the cell culture carriers taught by both Huguet & Dellacherie and Clapper et al are different than the instant invention, the method steps required to form layers of collagen and chitosan are same, and therefore, are immaterial to the benefits associated with such modification in the carrier for cell culture (as taught by Hara et al) using chitosan as an intermediate layer between alginate gel layer and collagen layer.

Since the benefits accruing from such a modification would provide an effective, biocompatible, reinforced support system for use in cell culture methods for mammalian cells that may require transfer of the cell culture product, lamination of the cultured cell layers, and formation of multilayered cell structures resulting in three-dimensional tissue structures (as disclosed by Hara et al, see column 7, first paragraph, in particular), one of ordinary skill in the art would be motivated to combine the teachings of the Huguet & Dellacherie and Clapper et al with the teachings of Hara et al to modify their carrier for cell culture (and hence the methods using that carrier) as claimed in the present invention.

As per MPEP, *"The selection of a known material based on its suitability for its intended use supported a prima facie obviousness determination in Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945)"* (see MPEP 2144.07).

Thus, the invention as a whole would have been *prima facie* obvious to one skilled in the art at the time the claimed invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyendra K. Singh whose telephone number is 571-272-8790. The examiner can normally be reached on 9-5MF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Satyendra K. Singh
Patent Examiner
Art Unit 1651

JEAN C. WITZ
PRIMARY EXAMINER